HALE AND DORR LLP
COUNSELLORS AT LAW

www.haledorr.com
THE WILLARD OFFICE BUILDING
1455 PENNSYLVANIA AVENUE, N.W. • WASHINGTON, D.C. 20004-1008
202-942-8400 • FAX 202-942-8484

MARK A. HELLER
202-942-8488
mark.heller@haledorr.com

October 19, 2000

Dockets Management Branch
(HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

RE: Previously submitted documents for inclusion in Docket Number 00P-0788

Dear Sir or Madam:

It has come to our attention that the following documents are not a part of the public record for the Petition for Reclassification of the Totally Implanted Spinal Cord Stimulator for Use in the Treatment of Chronic Intractable Pain. These documents, which were previously submitted by Medtronic to the FDA, are the kinds of materials that should be in the administrative record for this matter. See 21 CFR § 10.3(a) (defining "administrative record" as "the documents in the administrative file of a particular administrative action on which the Commissioner relies to support the action" and "administrative file" as "the file or files containing all documents pertaining to a particular administrative action, including internal working memoranda, and recommendations"). We are concerned that overheads from Medtronic's July 27, 2000 meeting have not been placed in the record as the company had specifically requested. See Medtronic's Aug. 14, 2000 letter to Dr. Pagano of ODE. Thus, we ask that the following documents be expeditiously placed in Public Docket Number 00P-0788. These documents, two copies of which are enclosed, are important to public opinion on this subject and should be available.

The enclosed documents for inclusion in the administrative record are:

- Aug. 9, 1999 Medtronic's Request to speak at Neurological Device Panel Sept. 17, 1999 in response to reclassification petition for Totally Implantable Pulse Generators (IPG's) for use in the treatment of chronic intractable pain

00P-0788

00D-1455

C20

- Aug. 23, 1999 Medtronic's response to Ms. Scudiero's request for a copy of Sec. 208 of the Food and Drug Administration Modernization Act of 1997, referenced in Medtronic's Aug. 9, 1999 letter

- Sept. 3, 1999 Medtronic's Response to petition to Neurological Advisory Panel September 17, 1999 for reclassification of Totally Implantable Spinal Cord Stimulator for use in the treatment of chronic intractable pain (with Attachments A-D)

- Sept. 17, 1999 Medtronic Response to Reclassification Petition (powerpoint presentation)

- Jan. 31, 2000 Medtronic's Petition for Reclassification of Totally Implantable Spinal Cord Stimulator for use in the Treatment of Chronic Intractable Pain (with Attachments A-D) [Please note that Attachment A is the ANS Petition which includes a copy of EN 45502-1. This copy, as provided by ANS, omits every other page of the standard.]

- June 12, 2000 Medtronic's Agenda for June 16, 2000 Meeting

- Aug. 14, 2000 Medtronic's Request that its July 27, 2000 Powerpoint Presentation be included in the Administrative Record

Thank you for including these documents in the public record. If there is any question regarding this request, please notify us at the above address or telephone us.

Sincerely,

Mark A. Heller

Mark A. Heller
Stephanie Philbin

Enclosures

Medtronic

Medtronic, Inc.
800 53rd Avenue N.E.
Minneapolis, MN 55421-1200 USA
www.medtronic.com

tel (612) 514-4000
toll free (800) 328-2518
fax (612) 514-4879

August 9, 1999

Janet L. Scudiero
Division of General and Restorative Devices
9200 Corporate Boulevard, HFZ-410
Rockville, MD 20850
Fax. (301) 594-2358

RE: Request to speak at Neurological Device Panel September 17, 1999 in response to reclassification petition for Totally Implantable Pulse Generators (IPG's) for use in the treatment of chronic intractable pain.

Dear Ms. Scudiero;

Medtronic is requesting the opportunity to make a presentation to the panel on September 17, 1999 in opposition to the petition requesting reclassification of Implantable Pulse Generators for the treatment of chronic intractable pain. We respectfully request - 45 minutes. Under section 513(b) (6)(iii) Medtronic believes as the current manufacturer we are entitled to equal time as the petitioner.

It is the opinion of Medtronic that there is not enough valid clinical and scientific data to support reclassification of this device. The petition advocates labeling and a limited standard as special controls to provide reasonable assurance of safety and effectiveness for the device as justification to move it from Class III PMA controls into Class II. The petition fails to show that those controls would be adequate to protect the public. The complexity of device with and its various applications (pacing, gastrointestinal, urinary, tremor and epilepsy, etc.) demand strong evidence demonstrating valid scientific data before reclassification should be permitted. Little if any valid scientific evidence supports the petition. We believe a case-by-case PMA review is necessary to protect the public safety and to provide reasonable assurance the device is safe and effective.

We believe this level of review/approval is paramount to protect the safety of the patients with the highly intricate specialized circuitry that is required to allow the power source to be internalized within this device. Also, the level of risk and the controls that are required to assure patient safety are greatly increased by the complexity of a totally implantable pulse generator.

The cost of a device failure could be significant to patients. Medtronic firmly believes that a product-by-product PMA review to protect consumers and premarketing inspections that accompany PMA approvals are necessary.

This required level of FDA review/approval for a Class III PMA device includes:

- Full premarket approval review before marketing,
- Full premarket approval review of changes requiring PMA supplements before marketing,
- Audit of manufacturing facilities prior to device approval,
- Rigorous review of bench, animal and clinical data, and
- Approval of comprehensive labeling prior to marketing.

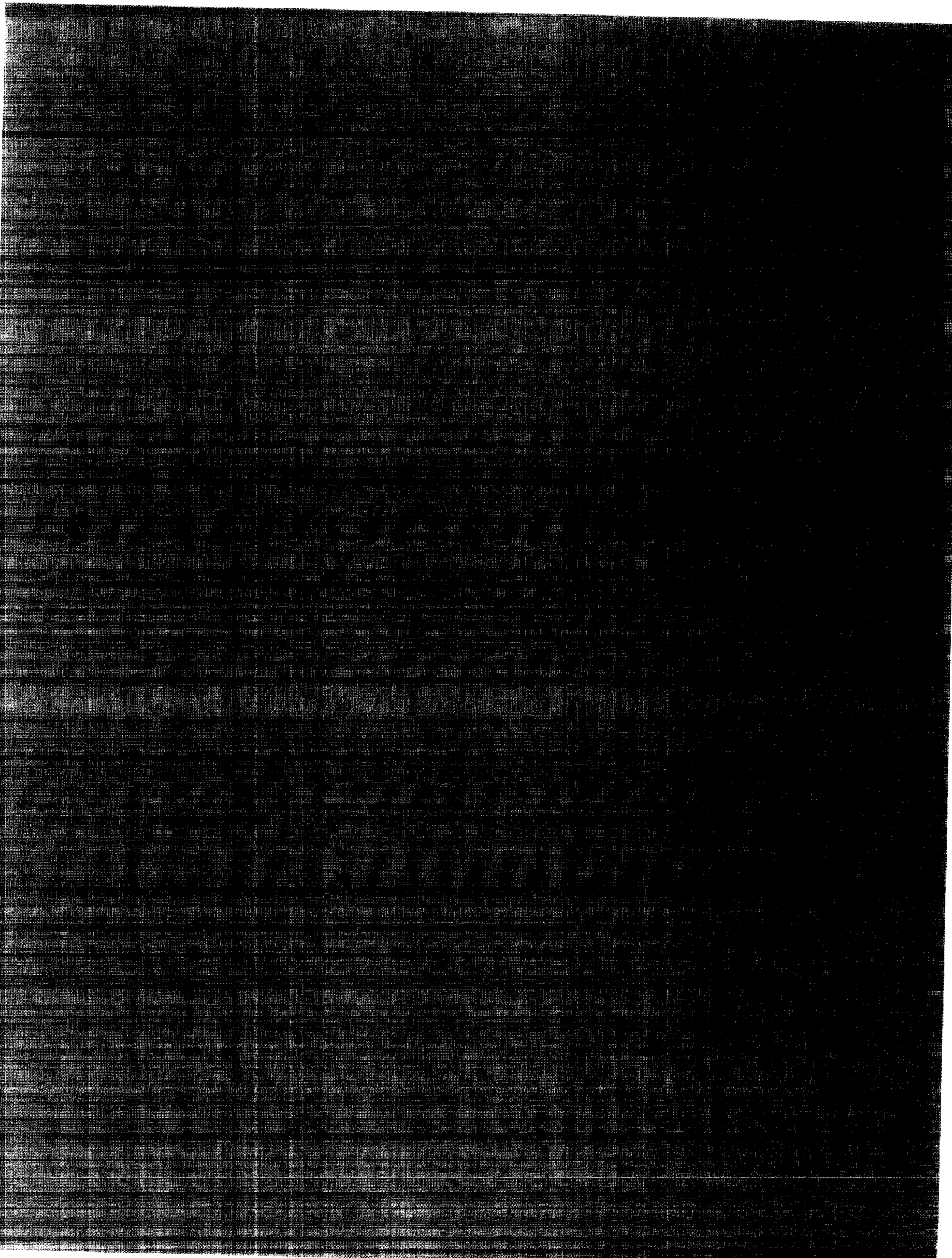
We believe the petitioner has not demonstrated reasonable assurance that an FDA Class II device classification, with "Special Controls" is sufficient to ensure safety and efficacy of devices within this classification. The reclassification will allow a significant loss in the amount of control, which are in place for the protection of the general public.

Prior to the panel meeting Medtronic will submit to the executive secretary of the neurological device panel a written statement of the company's views on the petition. Under 513(b)(6), we respectfully request this information be provided to the panel members for their consideration.

Thank you for your consideration of this request. If you have any additional concerns or questions please contact Kathy Jo Fahey at (612) 514-5198. In addition, we would appreciate FDA acknowledgement of receipt and concurrence with the above request to appear at the September panel and to have 45 minutes to present to the panel meeting.

Sincerely,
MEDTRONIC, INC. NEUROLOGICAL DIVISION

Lynn Switzer
RA/QA Director NeuroStim Business
(612) 514-7338
Fax (612) 514-5078
Email lynn.switzer@medtronic.com



FAX

Date 08-23-99

Number of pages including cover sheet 4

[redacted]

TO:	*Jan Scudiero*	***FROM:***	*Kathy Jo Fahey*
			Medtronic
cc.	*Russ Pagano*		*Neuro Division*
Phone	(301) 594-1184 ext.176	***Phone***	*(612) 514-5198*
Fax Phone	(301) 594-2358	***Fax Phone***	*(612) 514-5612*

CC:

REMARKS: ☐ *Urgent* ☒ *For your review* ☐ *Reply ASAP* ☐ *Please Comment*

Hello Jan,

As you requested attached is a copy of the section of the law referenced in Lynn Switzer's letter to you dated 8-9-99. The new section is from FDAMA. Please let me know as soon as you can what the decision is for time allowed for presentation at the September 17th panel, as well as a timeframe of additional information being submitted to the panel.

Best Regards,

Kathy

Kathy

2 of 7
8-23-94
K. Fahey

S. 830

One Hundred Fifth Congress of the United States of America

AT THE FIRST SESSION

Begun and held at the City of Washington on Tuesday, the seventh day of January, one thousand nine hundred and ninety-seven

An Act

To amend the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act to improve the regulation of food, drugs, devices, and biological products, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE; REFERENCES; TABLE OF CONTENTS.

(a) SHORT TITLE.—This Act may be cited as the "Food and Drug Administration Modernization Act of 1997".

(b) REFERENCES.—Except as otherwise specified, whenever in this Act an amendment or repeal is expressed in terms of an amendment to or a repeal of a section or other provision, the reference shall be considered to be made to that section or other provision of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301 et seq.).

(c) TABLE OF CONTENTS.—The table of contents for this Act is as follows:

(2) by adding at the end the following:

"(F) Not later than 270 days after the date of the enactment of the Food and Drug Administration Modernization Act of 1997, the Secretary shall issue guidance specifying the general principles that the Secretary will consider in determining when a specific intended use of a device is not reasonably included within a general use of such device for purposes of a determination of substantial equivalence under subsection (f) or section 520(l).".

SEC. 207. EVALUATION OF AUTOMATIC CLASS III DESIGNATION.

Section 513(f) (21 U.S.C. 360c(f)), as amended by section 206(b), is amended—

(1) in paragraph (1)—

(A) in subparagraph (B), by striking "paragraph (2)" and inserting "paragraph (3)"; and

(B) in the last sentence, by striking "paragraph (2)" and inserting "paragraph (2) or (3)";

(2) by redesignating paragraphs (2) and (3) as paragraphs (3) and (4), respectively; and

(3) by inserting after paragraph (1) the following:

"(2)(A) Any person who submits a report under section 510(k) for a type of device that has not been previously classified under this Act, and that is classified into class III under paragraph (1), may request, within 30 days after receiving written notice of such a classification, the Secretary to classify the device under the criteria set forth in subparagraphs (A) through (C) of subsection (a)(1). The person may, in the request, recommend to the Secretary a classification for the device. Any such request shall describe the device and provide detailed information and reasons for the recommended classification.

"(B)(i) Not later than 60 days after the date of the submission of the request under subparagraph (A), the Secretary shall by written order classify the device involved. Such classification shall be the initial classification of the device for purposes of paragraph (1) and any device classified under this paragraph shall be a predicate device for determining substantial equivalence under paragraph (1).

"(ii) A device that remains in class III under this subparagraph shall be deemed to be adulterated within the meaning of section 501(f)(1)(B) until approved under section 515 or exempted from such approval under section 520(g).

"(C) Within 30 days after the issuance of an order classifying a device under this paragraph, the Secretary shall publish a notice in the Federal Register announcing such classification.".

SEC. 208. CLASSIFICATION PANELS.

Section 513(b) (21 U.S.C. 360c(b)) is amended by adding at the end the following:

"(5) Classification panels covering each type of device shall be scheduled to meet at such times as may be appropriate for the Secretary to meet applicable statutory deadlines.

"(6)(A) Any person whose device is specifically the subject of review by a classification panel shall have—

"(i) the same access to data and information submitted to a classification panel (except for data and information that are not available for public disclosure under section 552 of title 5, United States Code) as the Secretary;

"(ii) the opportunity to submit, for review by a classification panel, information that is based on the data or information provided in the application submitted under section 515 by the person, which information shall be submitted to the Secretary for prompt transmittal to the classification panel; and

"(iii) the same opportunity as the Secretary to participate in meetings of the panel.

"(B) Any meetings of a classification panel shall provide adequate time for initial presentations and for response to any differing views by persons whose devices are specifically the subject of a classification panel review, and shall encourage free and open participation by all interested persons.

"(7) After receiving from a classification panel the conclusions and recommendations of the panel on a matter that the panel has reviewed, the Secretary shall review the conclusions and recommendations, shall make a final decision on the matter in accordance with section 515(d)(2), and shall notify the affected persons of the decision in writing and, if the decision differs from the conclusions and recommendations of the panel, shall include the reasons for the difference.

"(8) A classification panel under this subsection shall not be subject to the annual chartering and annual report requirements of the Federal Advisory Committee Act.".

SEC. 209. CERTAINTY OF REVIEW TIMEFRAMES; COLLABORATIVE REVIEW PROCESS.

(a) CERTAINTY OF REVIEW TIMEFRAMES.—Section 510 (21 U.S.C. 360), as amended by section 206(a)(2), is amended by adding at the end the following subsection:

"(n) The Secretary shall review the report required in subsection (k) and make a determination under section 513(f)(1) not later than 90 days after receiving the report.".

(b) COLLABORATIVE REVIEW PROCESS.—Section 515(d) (21 U.S.C. 360e(d)), as amended by section 202(1), is amended by inserting after paragraph (2) the following:

"(3)(A)(i) The Secretary shall, upon the written request of an applicant, meet with the applicant, not later than 100 days after the receipt of an application that has been filed as complete under subsection (c), to discuss the review status of the application.

"(ii) The Secretary shall, in writing and prior to the meeting, provide to the applicant a description of any deficiencies in the application that, at that point, have been identified by the Secretary based on an interim review of the entire application and identify the information that is required to correct those deficiencies.

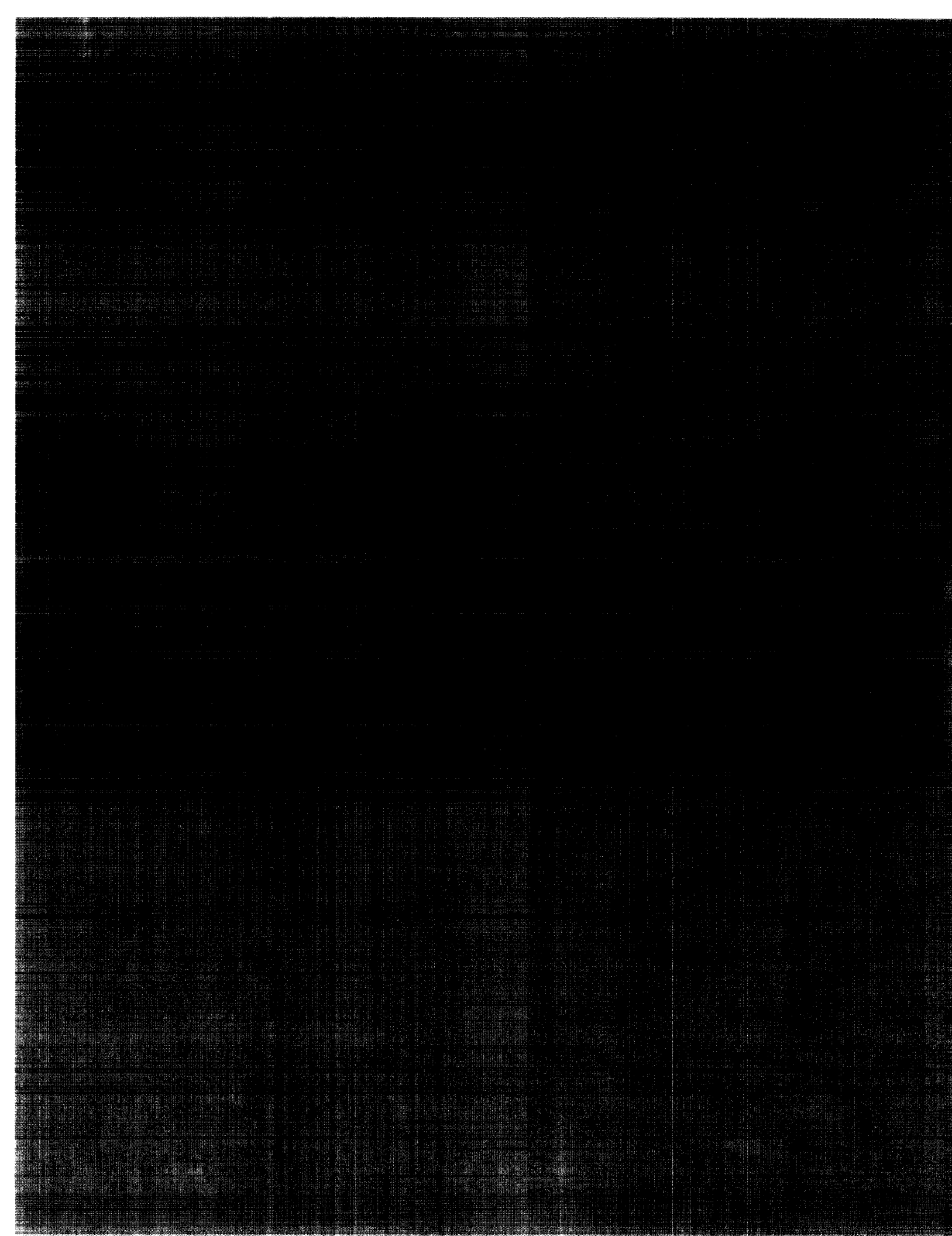
"(iii) The Secretary shall notify the applicant promptly of—

"(I) any additional deficiency identified in the application, or

"(II) any additional information required to achieve completion of the review and final action on the application,

that was not described as a deficiency in the written description provided by the Secretary under clause (ii).

"(B) The Secretary and the applicant may, by mutual consent, establish a different schedule for a meeting required under this paragraph.



Medtronic, Inc.
800 53rd Avenue N.E.
Minneapolis, MN 55421-1200 USA
www.medtronic.com

tel 612.514.5000
tel 800.328.0810
fax 612.514.5078

September 3, 1999

Janet L. Scudiero
Division of General and Restorative Devices
9200 Corporate Boulevard, HFZ-410
Rockville, MD 20850
Fax. (301) 594-2358

RE: Response to petition to Neurological Advisory Panel September 17, 1999 for reclassification of Totally Implantable Spinal Cord Stimulator for use in the treatment of chronic intractable pain.

Dear Ms. Scudiero;

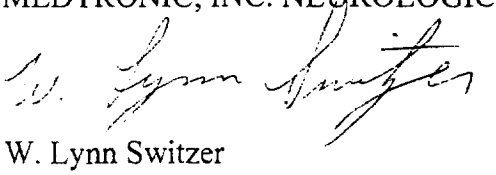
Enclosed are twenty (20) copies of Medtronic's response to the petition for reclassification of Totally Implantable Spinal Cord Stimulators that will be presented at the September 17, 1999 Neurological Advisory Panel. Under 513(b)(6) we respectfully request that this information be provided to the panel members and FDA for their consideration prior to the meeting.

We wish to reiterate our belief that the petitioner has not demonstrated reasonable assurance that an FDA Class II device classification with "Special Controls" is sufficient to ensure the safety and efficacy of devices within this classification. The proposed reclassification would allow a significant loss in the controls that are in place for the protection of the general public. We believe our response will aid the panel members in their determination to retain the Class III designation for the "Totally Implantable Spinal Cord Stimulator for the use in the treatment of chronic intractable pain."

Medtronic provides this information for the FDA Neurological Advisory Panel and believes to the best of our knowledge that all data and information submitted are truthful and accurate and no material fact has been omitted. Medtronic acknowledges that this document's contents are subject to, and comply with, 18 U.S.C. 1001, chapter 47, Fraud and False Statements; as well as with 18 U.S.C. 1515, chapter 73, Obstruction of Justice (for a proceeding before a federal government agency).

Thank you for your time in reviewing this response. If you have any additional concerns or questions please contact the undersigned or Kathy Jo Fahey at (612) 514-5198.

Sincerely,
MEDTRONIC, INC. NEUROLOGICAL DIVISION



W. Lynn Switzer
RA/QA Director NeuroStim Business
(612) 514-7338
Fax (612) 514-5078
Email: lynn.switzer@medtronic.com

Table of Contents

Attachments

A. Letter from Dr. Henney
B. Letter from Dr. Alpert
C. Bibliography
D. Literature Table

The impact to patients of a device failure could be significant. Medtronic firmly believes that a product-by-product PMA review, and the premarketing inspections that accompany PMA approvals, are necessary to protect consumers.

Prior to marketing, the required level of FDA review/approval for a Class III PMA device includes:

- Full premarket approval review,
- Full premarket approval review of changes requiring PMA supplements,
- FDA inspection and audit of manufacturing facilities,
- Rigorous review of bench, animal and clinical data, and
- Approval of comprehensive labeling.

Examples of how the system works to protect the public (e.g. warning letters and 483 observations)

The current classification and the related FDA review and approval on a case-by-case basis has resulted in the protection of public health.

Patient risks can be identified from both technological issues and actual events. From a technical standpoint, there are significant issues in the attempted validation of an implanted power source, e.g., insulation materials, hybrid circuit, feed-throughs, titanium can sealing, electrical and welding specifications, and battery sealing.

Examples of attempted commercialization of neurostimulators include one neurostimulation company's development of a totally implantable generator (IPG) that was not successful because of the failure of the battery and (its associated control circuitry) manufacturing methods, and facilities. The resulting patient injuries were significant.

The risks to human health were so significant that FDA had to terminate the company's IDE clinical study because the "unreasonable risk to public health owing to the inadequacy of the methods, facilities, and controls used in the manufacture of the device."

This device's technological failures included:

- Fluid leakage into the device causing battery failure (loss of hermetic seal),
- Battery failure due to insufficient or no welding,
- Battery feed throughs' performance and process validation not documented,
- Inadequate battery cell and battery outer can validation/ qualification testing,
- High battery impedance,
- Transient programmer failure,
- Battery insulation redesigned and implemented, but not qualified and no FDA notification or approval,
- Programmer/ Transmitter circuitry redesigned and implemented, but not qualified, and no FDA notification or approval,

This company's clinical usage of the device with patient injuries included:

- Not reporting patient injuries (such as **"shocks", "getting zapped", or "electrical shocks"**) to FDA via MDR or IDE,
- Not reporting to FDA Unanticipated Adverse Device Effects, such as **"intolerable increase in stimulation", "increased stimulation to intolerable levels", and "battery thoroughly discharged**."

These failures demonstrate actual patient harm, as well as the increased risk inherent in the devices. These observations would not have been discovered if not for the pre-approval inspection of the manufacturing site.

A second **neurostimulation** company's attempt to design and manufacture an implanted device with internal battery also failed. This device failed because issues relating to the battery and its technology resulted in patient harm. This battery's electrolytes diffused through its silicone holder, i.e., the electrolytes leaked within the implanted device. This leakage caused the control circuit to fail, which in turn caused the device to either (a) not be programmable (not able to turn off the device), (b) change parameters on its own, or (c) cease functioning. At a minimum all of the failures resulted in device explant, and some in patient harm.

Since totally implantable IPG technology is very similar between neurostimulators and pacemakers, pacemakers can also be reviewed for risks of technology failures:

- The loss of the hermetic seal, (the battery feed through had a glass to metal seal which failed) in one **pacemaker** company's devices, resulted in the battery shorting out within 4 to 18 months.
- Another **pacemaker** company issued a safety alert for pacemakers which could fail without warning due to the loss of "hermeticity" because of cracked ceramic feed throughs or separation of a braze joint between ceramic and titanium components, resulting in fluid ingress into the pacemaker.

3. Technical Discussion

As stated previously, the "addition of a battery" is written by the petitioner as if one is placing batteries in a flashlight. As multiple manufacturers have discovered this is not the case. The technological issues and hazards (those that have resulted in patient injury and harm) have demonstrated the vast complexities of such devices and the requirement to review each manufacturer's device on a case-by-case basis.

What is necessary to internalize the battery is not the only difference between an IPG and a Radiofrequency system. A comparison of RF receivers and IPGs follows:

Table 1: Comparison of RF and IPG Devices

RF Devices –(Receiver only implanted)	**IPG (with battery)**
Antenna to receive **power**	Antenna to receive **communication**
Circuit = Simple remodulator and switch circuit Does **NOT**: 1. Generate stimulation pulses 2. Control stimulation parameters	Circuit = 1. Generates pulses 2. Controls stimulation parameters 3. Self-contained system 4. Reliability important because may not turn off when desired (vs. simply removing RF antenna)
Encapsulation = epoxy	Container = Titanium
No Internal Power Source, Power received from external transmitter	Internal Power Source 5. Large amount of chemical energy 6. Potential for electrical shorts 7. Potential for heating 8. Potential for battery chemical leaks 9. Potential for fluid leakage into battery 10. Extensive manufacturing controls required 11. Potential explosive reactions
Emergency Stop = Remove external transmitter Antenna	Emergency Stop = Requires either: • Programmer telemetry or • Communication with IPG or • Emergency explant
Engineering Design = Simple	Engineering Design = Complex
Manufacturing = Simple	Manufacturing = Complex

There are no FDA guidance documents on the appropriate testing of implantable pulse generators, with internal power sources. For Class III devices, it is up to the manufacturer to submit data demonstrating safety and effectiveness. For Class II devices, the manufacturer only has to demonstrate "substantial equivalence" (510(k) approval) to a pre-1976 device. or to one that has already received 510(k) approval.

Examples of the differences in testing are as follows:

Table 2: Medtronic Testing Requirements - Differences

RF Devices –(Receiver only implanted)	**IPG (with battery)**
N/A	Battery - Electrical discharge testing - Longevity at nominal outputs
N/A	Hybrid Circuit testing - Current Drain - Rate limit - Circuit Signal and converter - Battery monitor - Battery End of Life threshold Integrated Circuit Testing - Telemetry linkage - Signal converter - Power on Reset
N/A	Programmer Testing - Software - Keyboard - Programming Wand - Components - Function/ Telemetry capability - Mechanical shock and vibration
Software Testing	Software Compatibility
Incompatible Transmitter Interaction	Programmer Compatibility

Table 3: Medtronic Testing Requirements - Similarities

RF Devices –Implanted Receiver	IPG (with battery)
Stimulation Parameter testing (Amplitude, Rate, Pulse Width)	Stimulation Parameter testing (Amplitude, Rate, Pulse Width)
Electrical Tests - Power up power on reset - Amplitude calibration / max. limit - Electrode programming/ channel - Net DC Current - Rate range - Pulse width range - Signal cross talk - Stimulation disable - Receiver implant depth max. - Receiver/ antenna offset max. - Multiple systems interaction	Hybrid Circuit testing - Rate - Pulse width - Output pulse - Switches - Circuit components - Burn in Integrated Circuit testing - Timing and interface - Voltage reference - Failure modes - EMC - System compatibility - In-vitro test systems
Biocompatibility Testing	Biocompatibility Testing
Electromagnetic Compatibility (EMC) Testing	Electromagnetic Compatibility (EMC) Testing
Environmental Stress, e.g., mechanical shock and vibration	Environmental Stress, e.g., mechanical shock and vibration
Connector Testing, e.g., fluid leakage and impedance	Connector Testing, e.g., fluid leakage and impedance
Extension and Lead Testing	Extension and Lead Testing

4. <u>Medical Device Reporting (MDR)</u>

A search of the MDR database was performed using Medline and Diogenes. The specified parameter was "spinal cord stim". This search resulted in reports dated from April 14, 1981 to December 1,1998. There were 2299 entries, of which 780 were specific reports on implantable pulse generator (IPG) or radio frequency (RF) devices. There are three MDR Categories: death, serious injury and malfunction. There was one death reported (0.10%), 305 serious injuries (39%) and 474 malfunctions (61%). The definitions of the last two FDA categories are provided for reference.

"Serious Injury/(Serious illness) [§803.3(a)(1)]

- Is life threatening, even if temporary in nature;
- Results in permanent impairment of a body function or permanent damage to a body structure; or

- Necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure."

"Malfunction [§803.3(m)]
A "malfunction" is a failure of the device to meet its performance specifications or otherwise perform as intended. Performance specifications include all claims made in the labeling for the device. A malfunction should be considered reportable if any one of the following is true:

- The chance of a death or serious injury resulting from a recurrence of the malfunction is not remote;
- The consequences of the malfunction affect the device in a catastrophic manner that may lead to a death or serious injury;
- The malfunction causes the device to fail to perform its essential function and compromises the device's therapeutic, monitoring or diagnostic effectiveness (emphasis provided by Medtronic) **Which could cause or contribute to a death or serious injury, or other significant adverse device experiences. The essential function of a device refers not only to the device's labeled use, but for any use widely prescribed within the practice of medicine;**
- **The malfunction involves a long-term device implant that would prevent the implant from performing its function;**
- **The device is considered life-supporting or life-sustaining, and thus essential to maintaining human life;** or
- The manufacturer takes or would be required to take action under section 518 or 519(f) of the FD&C Act as a result of the malfunction of the device or other similar devices."

It is essential to remember the underlined portion above when reviewing this reclassification petition. Consideration should be given to the fact that an IPG can be prescribed for other stimulation therapies besides Spinal Cord Stimulation (SCS). A physician may deem a stimulation system medically necessary and prescribe it for other anatomical locations or symptoms of disease such as cardiac pacing, gastrointestinal and urinary disorders, and tremor and epilepsy.

The reports by company, model number and type of event were reviewed and are reported in Tables 4 through 6.

The MDRs were also reviewed by type of event. These were placed into eight categories: device malfunction, battery, programming, stimulation, patient sequelae, elective removal, improper implant procedure, and explanted – unknown reason.

The single death that was reported was due to meningitis and text from this report is contained within the MDR "sample text" section of this document. The most frequently reported event was "no output" at 160/780 (21%). Intermittent stimulation at 136/780 (17%) was the next most frequently reported event. Device malfunction at 132/780 (17%) had a similar number of events reported.

Within the category of patient sequelae, the most frequently reported event was infection 33/780 (4%). Pain was reported in 10/780 (1%) of MDR events. All of the above events resulted in the patient undergoing an additional operative procedure in which the device was explanted.

The petitioner has failed to recognize many MDR reported events related to these devices. On page of 14 of this document are examples of MDR text in which the respective manufacturers reported the events. This text is provided to show evidence of events that can occur with an internal battery. The petitioner has suggested that battery depletion is the only issue related to an internal battery, although the battery has caused reportable events, not all are due to increased voltage which minimizes the life of the battery. The petitioner has suggested labeling would be an adequate control for this occurrence. Medtronic concurs; in fact we have already implemented such labeling. However, the MDR text describes additional events which affect the battery such as: a hybrid failure resulting in a current drain, a discrepant control gate also resulting in a current drain and in a possible battery leak. None of these events would have been resolved or minimized by the proposed labeling control. They clearly demonstrate the need for additional bench testing for IPGs (see Table 2, page 6).

It is also important to take note of the number of "programming" events that were reported: 228/780 (29%), approximately a third of all the MDRs reviewed. As stated previously all of these events resulted in the device being explanted. Since the circuitry required to internalize the battery is complex, if there is an issue with programming the device, (e.g., no telemetry, turning on and off on its own, no output or simply not able to program,) in most instances the resolution is to explant the device. For RF devices, programming occurs in the external portion of the system and can be easily remedied with repair or exchange of the external unit.

Likewise, if a device is delivering intermittent stimulation or surges, (and in some cases shocks), the device may have lost its capability to respond to the physician/patient programmer and it may not be possible to turn the device off. In these instances, the only resolution again is emergency surgical removal of the device. The labeling and limited standard controls proposed by the petitioner would be inadequate to minimize these occurrences. To restate, we as a current manufacturer of these devices, have, with the assistance of FDA, instituted significant and rigorous clinical and non-clinical testing to assure that occurrences such as these are minimized prior to commercial release of the product.

The subject of this response as well as the subject of the petitioner's request for reclassification is the totally implantable spinal cord stimulator. The petitioner has included MDR reports unrelated to this device. We have chosen not to include MDR reported events for lead migration, epidural hemorrhage, seroma, paralysis, cerebral spinal fluid leak, lead breakage, or loose connection in our review, differing from the

petitioner's analysis, since these were due to the interaction or failure of the lead and/or extension.

The MDR database does not capture all events, as evidence of the fact is our review of the FDA regulatory actions, a FDA 483 observations had noted that the manufacturer/sponsor of an Investigational Device Exemption (IDE) had not reported events as required by regulation.

Table 4: Type of MDR by Manufacturer

	Medtronic	Neuromed	Cordis	EBI Medical Systems	Total
Death	0	1	0	0	**1**
Serious Injury	181	106	15	3	**305**
Malfunction	199	261	14	0	**474**
Total	**380**	**368**	**29**	**3**	**780**

Table 5a: MDR Type by Manufacturer; by Model #: *Medtronic*

Model	Death	Serious Injury	Malfunction	Total
3272	0	6	1	**7**
3360	0	2	5	**7**
3462/3463	0	0	2	**2**
3464/3465	0	6	21	**27**
3470	0	22	2	**24**
7420/7421	0	10	88	**98**
7424	0	133	80	**213**
7425	0	2	0	**2**
Total	**0**	**181**	**199**	**380**

Table 5b: MDR Type by Manufacturer; by Model #: *Neuromed*

Model	Death	Serious Injury	Malfunction	Total
TI-94	0	6	2	8
MNR4	0	0	3	3
MNR881	0	0	1	1
MNR88	0	46	128	174
MNR98	0	8	0	8
MNR916	0	17	0	17
MNR94	0	18	126	144
MNR944	0	2	0	2
MNR948	0	2	0	2
MBR88	0	1	0	1
MNT4D	0	1	0	1
MNT46	0	1	0	1
MNT88D	0	0	1	1
MCR88	0	1	0	1
Custom Device	0	1	0	1
Unknown	1	2	0	3
Total	**1**	**106**	**261**	**368**

Table 5c: MDR Type by Manufacturer; by Model #: *Cordis*

Model	Death	Serious Injury	Malfunction	Total
Mark II- 940D	0	15	14	29
Total	**0**	**15**	**14**	**29**

Table 5d: MDR Type by Manufacturer; by Model #: *EBI Medical Systems*

Model	Death	Serious Injury	Malfunction	Total
10-1332W	0	2	0	2
10-1370W	0	1	0	1
Total	**0**	**3**	**0**	**3**

Table 6: Overall MDR Report by Type of Event

Type of Event	Death	Serious Injury	Malfunction	TOTAL
Device Malfunction				
Malfunction	0	65	67	**132**
Connector or adaptor passage clogged or blocked	0	1	0	**1**
Signs of fluid intrusion and signs of rust in setscrews	0	7	11	**18**
Battery				
End of life/battery depletion	0	13	49	**62**
Leakage – from battery pack	0	2	0	**2**
Programming				
Programming	0	10	21	**31**
No Telemetry	0	3	9	**12**
Turning on or off next to power lines	0	0	1	**1**
Turning on or off on its own	0	14	10	**24**
No output	0	21	139	**160**
Stimulation				
Unsatisfactory Stimulation	0	10	29	**39**
Erratic Stimulation	0	2	1	**3**
Intermittent stimulation/no stimulation	0	68	68	**136**
Overstimulation while passing through security system	0	1	9	**10**
Greater stimulation than anticipated	0	5	4	**9**
Surging	0	5	13	**18**
Strong surges of stimulation	0	2	0	**2**
Surging, Shocking, jabbing jerking movements	0	9	0	**9**
Jolts around implant site and legs	0	2	3	**5**
Shock	0	4	6	**10**
Severe shock	0	1	0	**1**
Massive shock	0	1	0	**1**
Electrical failure	0	1	1	**2**

Type of Event	Death	Serious Injury	Malfunction	TOTAL
Fluctuations in amplitude	0	0	2	**2**
Runaway amplitude	0	1	0	**1**
Abnormal heartbeat	0	1	0	**1**
Vibration	0	1	0	**1**
Short Circuit	0	0	2	**2**
Patient Sequelae				
Constant burning pain	0	2	2	**4**
Alleged permanent disability	0	1	0	**1**
Patient injury	0	7	2	**9**
Pain	0	4	6	**10**
Infection	0	20	13	**33**
Swollen implant pocket	0	1	0	**1**
Hematoma at implant site	0	1	0	**1**
Pocket healing	0	2	1	**3**
Death	1	0	0	**1**
Elective removal	0	6	1	**7**
Improper implant procedure – device explanted	0	2	1	**3**
Explanted – unknown reason	0	9	3	**12**
TOTAL	**1**	**305**	**474**	**780**

Examples of MDR text:

Death

TX - TEXT: A PT, WHOSE HEALTH WAS DETERIORATING RAPIDLY, WAS IMPLANTED WITH A STIMULATOR ON 1/30/96. AFTER A 15 DAY TRIAL THE PT WAS DIAGNOSED WITH MENINGITIS AND PASSED AWAY ONE WEEK LATER. THE DEVICE HAS NOT BEEN RETURNED TO THE MFR FOR EVAL. BASED ON THE ONLY INFORMATION CO HAS RECEIVED, CO DOES NOT FEEL THAT THERE IS ENOUGH INFORMATION TO SUGGEST THAT CO'S PRODUCT CONTRIBUTED OR CAUSED THE PT'S DEATH. IN CO'S LITERATURE FOR THE PHYSICIAN IT STATES THAT IT IS NOT RECOMMEDED ON PATIENTS WHO HAVE RAPIDLY PROGRESSING DISORDER.
DT - DATE OF OCCURRENCE: 19960329
AN - ACCESSION NUMBER: 1551242

Battery

TX - TEXT: THE DEVICE WAS EXPLANTED DUE TO REPORTED **"BATTERY DEPLETION", HOWEVER, ANALYSIS REVEALED A HIGH CURRENT DRAIN FROM THE HYBRID CAUSED BY A LEAKY N-CHANNEL TRANSISTOR** IN THE ANTENNA DRIVEN CIRCUIT OF THE L44 IC.
DT - DATE OF OCCURRENCE: 19960418
AN - ACCESSION NUMBER: 1555967

TX - TEXT: FOREIGN MFR NO LONGER IN BUSINESS. THE RECEIVER WAS EXPLANTED AND RETURNED TO CO ON 10/9/92 WITH A CLAIM THAT THE **PT EXPERIENCED A SWOLLEN POCKET AND STRONG ELECTRICAL SURGES EVEN WHEN THE IMPLANT WAS TURNED OFF. UPON EXPLANT, THE POCKET WAS FULL OF NECROTIC TISSUE EVIDENTLY CAUSED BY A BLACKISH GREEN EXUDATE COMING FROM THE NECK OF THE IMPLANT.** THE BATTERY HAS BEEN SENT TO THE MFR FOR FURTHER ANALYSIS. A FINAL REPORT WILL BE FORWARDED UPON CONCLUSION OF ANALYSIS. THE CAUSE OF THIS EVENT HAS NOT BEEN DETERMINED. IN ADDITION, AVAILABLE FREQUENCY AND SEVERITY DATA DO NOT INDICATE THAT ANY FURTHER INVESTIGATION IS NECESSARY AT THIS TIME. BOTH THE FREQUENCY AND SEVERITY OF THIS EVENT WILL BE PERIODICALLY MONITORED TO DETERMINE IF ANY FOLLOW-UP AND/OR OTHER ACTION IS INDICATED.
DT - DATE OF OCCURRENCE: 19921215
AN - ACCESSION NUMBER: 1211057

TX - TEXT: PRODUCT WAS RETURNED TO CO FOR EVALUATION WITH A COMPLAINT OF "DEFECTIVE, MALFUNCTIONING". NO PT COMPLICATIONS OR PROBLEMS WERE REPORTED. THE COMPLETED VENDOR ANALYSIS WAS RECEIVED BY CO ON 9/15/89. ALTHOUGH THE UNIT DID MEET THE MINIMUM BATTERY CELL LIFE REQUIREMENTS BASED ON IMPLANT AND EXPLANT INFO RECEIVED FROM THE CUSTOMER, A **DISCREPANT CURRENT CONTROL GATE WAS DETECTED ON ANALYSIS. THIS RESULTED IN AN OUTPUT VOLTAGE WHICH WAS OUT OF SPECIFICATIONS AND A CURRENT DRAIN WHICH WAS HIGH FOR THE PROGRAMMED PARAMETERS.** THIS REPORT WAS REVIEWED FOR SIGNIFICANT PROBLEMS BUT WAS NOT CLOSED. IT IS BEING CLOSED AT THIS TIME AS PART OF A BATCH CLOSEOUT PROCESS IN ORDER TO PREPARE THE DATABASE TO SERVE AS HISTORICAL SUPPORT TO A REDESIGNED DATABASE.
DT - DATE OF OCCURRENCE: 19891005
AN - ACCESSION NUMBER: 1083292

Stimulation

TX - TEXT: FOR THE PAST YEAR **PT HAS EXPERIENCED PRICKLY SENSATION OR NO STIMULATION WHEN DEVICE IS ON. STIMULATION HAS THROWN PT DOWN SEVERAL TIMES WHEN STIMULATION COMES ON. DEVICE HAS NOT WORKED AT ALL FOR THE PAST TWO MONTHS.** THE DEVICE WAS EXPLANTED. EXPLANT DATE: 3/24/96. DEVICE NOT RETURNED TO MFR.
DT - DATE OF OCCURRENCE: 19960405
AN - ACCESSION NUMBER: 1553145

Fluid Intrusion

TX - TEXT: THE RECEIVER WAS EXPLANTED AND **SIGNS OF FLUID INTRUSION WAS FOUND IN THE RECEIVER. THERE WERE ALSO SIGNS OF RUST FOUND IN SETSCREWS.** THE RECEIVER HAS NOT YET BEEN RETURNED TO CO FOR ANALYSIS. A FINAL SUMMARY ANALYSIS WILL BE PROVIDED TO FDA WITHIN 120 DAYS UPON THE RETURN OF THE DEVICE.
DT - DATE OF OCCURRENCE: 19950908
AN - ACCESSION NUMBER: 1486856

TX - TEXT: THE RECEIVER WAS EXPLANTED AND RETURNED TO CO ON 6/15/93 DUE TO RECEIVER MALFUNCTION. A PRELIMINARY MDR, DATED 6/18/93, WAS SENT TO FDA. VISUAL EXAMINATION **REVEALED SIGNS OF FLUID INFILTRATION, AS THE HYBRID LABEL APPEARED WRINKLED. THERE WERE ALSO SIGNS OF FLUID INTRUSION INTO TERMINAL BLOCKS 1 AND 5 WICKING DOWN THE HYBRID LEADS TO THE HYBRID. THERE WAS ALSO SOME DISCOLORATION OF THE HYBRID NEAR LEADS 6, 7 AND 8 ON THE "A" HYBRID AND NEAR LEAD #1 OF THE "B" HYBRID.** THERE WERE NO SIGNS OF BOOT LEAK. ELECTRICALLY THE RECEIVER WOULD NOT PASS AUTOTESTING. FAILURE DUE TO FLUIDS BEING TRAPPED DURING THE IMPLANT PROCEDURE AND EVENTUALLY WICKING DOWN AND CAUSING THE HYBRID TO ELECTRICALLY MALFUNCTION.
DT - DATE OF OCCURRENCE: 19930726
AN - ACCESSION NUMBER: 1289958

No Output

TX - TEXT: THE DEVICE WAS EXPLANTED DUE TO **"NO OUTPUT."** THIS DEVICE WAS MFG AND DISTRIBUTED OUTSIDE THE US. ANALYSIS REVEALED A HIGH CURRENT DRAIN ON THE HYBRID.
DT - DATE OF OCCURRENCE: 19950202
AN - ACCESSION NUMBER: 1448216

Electrical Failure

TX - TEXT: THE RECEIVER AND LEAD WAS EXPLANTED AND RETURNED TO CO ON 5/6/94 WITH A CLAIM THAT THE DEVICE WAS MALFUNCTIONING. **ANALYSIS REVEALED THERE WAS ELECTRICAL FAILURE OF THE RECEIVER, SPECIFICALLY THE HYBRID.**
DT - DATE OF OCCURRENCE: 19940727
AN - ACCESSION NUMBER: 1409253

Programming

TX - TEXT: NEURAL STIMULATOR WAS EXPLANTED AFTER 4 MONTHS DUE TO REPORT THAT **THE PATIENT SUSTAINED A FALL THAT APPEARS TO HAVE RESULTED IN AN INABILITY TO TURN THE STIMULATOR OFF.** SOMETIME LATER, THE NEURAL STIMULATOR REPORTEDLY QUIT ON ITS OWN. NO OTHER INFORMATION IS AVAILABLE. THE NEURAL STIMULATOR WAS REPLACED UNEVENTFULLY WITH A NEW CORDIS UNIT WITHOUT REPORT OF PATIENT INJURY OR COMPLICATION. PATIENT CONDITION IS REPORTED AS SATISFACTORY. THE EXPLANTED STIMULATOR IS TO BE RETURNED TO CORDIS FOR ANALYSIS. THE CAUSE OF THIS EVENT HAS NOT BEEN DETERMINED. IN ADDITION, AVAILABLE FREQUENCY AND SEVERITY DATA DO NOT INDICATE THAT ANY FURTHER INVESTIGATION IS NECESSARY AT THIS TIME. BOTH THE FREQUENCY AND SEVERITY OF THIS EVENT WILL BE PERIODICALLY MONITORED TO DETERMINE IF ANY FOLLOW-UP AND/OR OTHER ACTION IS INDICATED.
DT - DATE OF OCCURRENCE: 19870130
AN - ACCESSION NUMBER: 1038892

TX - TEXT: THE DEVICE WAS EXPLANTED AND RETURNED DUE TO DIFFICULTIES IN PROGRAMMING. **FAILURE ANALYSIS REVEALED A COLD SOLDER JOINT AT THE CONNECTION BETWEEN THE TWO HYBRIDS.** THE CAUSE OF THIS EVENT HAS NOT BEEN DETERMINED. IN ADDITION, AVAILABLE FREQUENCY AND SEVERITY DATA DO NOT INDICATE THAT ANY FURTHER INVESTIGATION IS NECESSARY AT THIS TIME. BOTH THE FREQUENCY AND SEVERITY OF THIS EVENT WILL BE PERIODICALLY MONITORED TO DETERMINE IF ANY FOLLOW-UP AND/OR OTHER ACTION IS INDICATED.
DT - DATE OF OCCURRENCE: 19940322
AN - ACCESSION NUMBER: 1371922

Patient Injury

TX - TEXT: LEGAL DEPT RECEIVED A TELEPHONE CALL FROM AN INDIVIDUAL WHO IDENTIFIED HIMSELF AS BOTH A PHYSICIAN AND THE PT ASSOCIATED WITH THE COMPLAINT. **THE PT REPORTED THAT HE HAD RECENTLY HAD HIS NEUROSTIMULATOR AND LEADS EXPLANTED APPROX 9 YRS POST-IMPLANT. THE ALLEGED REASONS GIVEN FOR EXPLANT INCLUDED MULTIPLE MEDICAL PROBLEMS RESULTING FROM SILICONE LEAKAGE FROM THE BATTERY PACK AND LEADS. THE PT INDICATED THAT HE DEVELOPED DUPUYTREN'S CONTRACTURES, ARTHRITIS, PEYRONIE'S DISEASE AND URTICARIA APPROX 4 YRS PRIOR TO THE EXPLANT. TREATMENT OF THE MMP'S INCLUDED ADMINISTRATION OF STEROIDS (UP TO 60MG/GD), WHICH CONTINUES AT PRESENT.** PT INDICATED THAT HE WENT OUT ON DISABILITY 9 YRS PRIOR DUE TO A LOWER BACK INJURY, AT WHICH TIME THE NEUROSTIMULATOR WAS IMPLANTED. APPROX 4 REVISIONS WERE PERFORMED ON THE IMPLANT FOR LEAD AND POCKET PROBLEMS. THE EXPLANTING PHYSICIAN WAS CONTACTED AND INDICATED THAT THE SYSTEM WAS EXPLANTED PER THE PT'S REQUEST AS AN ELECTIVE PROCEDURE. THE PT HAS INDICATED THAT HE WOULD LIKE TO AVOID LITIGATION ON THIS ISSUE AND IS REQUESTING COMPENSATION FOR ALL HIS MEDICAL BILLS. THIS IS THE FIRST SUCH CASE RECEIVED ALLEGING INJURY RESULTING FROM IMPLANTABLE SILICONE DEVICES. THE PT IS IN POSSESSION OF THE EXPLANTED DEVICES AND HAS NOT INDICATED THAT THEY WILL BE RETURNED FOR EVALUATION AND TESTING. DURING THE DEVELOPMENT AND MFG OF BOTH THE PACING AND NEURO PRODUCTS, CO DID EXTENSIVE TESTING ON THE SILICONE PRODUCTS FOR BIOCOMPATIBILITY. THE SILICONE USED IN THESE PRODUCTS, UNLIKE THAT IN A GEL FORM, IS FULLY CURED, WITH A HIGH MOLECULAR WEIGHT, SUCH THAT ONE WOULD NOT ANTICIPATE ANY MIGRATION OF SILICONE. THIS IS SUPPORTED BY THE TEST RESULTS MEETING OR EXCEEDING THE USP STANDARDS FOR LEACHABLES.
DT - DATE OF OCCURRENCE: 19931222
AN - ACCESSION NUMBER: 1323755

TX - TEXT: A PT IMPLANTED WITH AN IMPLANTABLE PULSE GENERATOR WAS BEING DISCHARGED FROM THE HOSP. **UPON ENTERING THE AUTO FOR THE TRIP HOME, HE MOVED THE BAG CONTAINING THE MAGNETS ACROSS HIS LAP AND TURNED THE PULSE GENERATOR ON. A STRONG MOTOR RESPONSE WAS ELICITED WHICH CAUSED HIM TO JAM HIS LEG INTO THE DASH AND CAUSED A FRACTURE OF THE FEMUR HEAD. HE SUBSEQUENTLY HAD A PROSTHETIC HIP IMPLANT.** THERE ARE NO PLANS TO EXPLANT THE SYSTEM AT THIS TIME.
DT - DATE OF OCCURRENCE: 19930113
AN - ACCESSION NUMBER: 1240594

Shocking/Jolting

TX - TEXT: THE ANTENNA REPORTEDLY "SHORTED". **THE PT REPORTED HE RECEIVED A JOLT WHILE DRIVING HIS CAR CAUSING AN ACCIDENT.** THERE WAS NO INJURY HOWEVER IT COULD CAUSE OR CONTRIBUTE TO AN INJURY IF THE MALFUNCTION WERE TO RECUR. ANALYSIS REVEALED A BROKEN WIRE AT THE CONNECTOR END.
DT - DATE OF OCCURRENCE: 19931021
AN - ACCESSION NUMBER: 1318906

TX - TEXT: THE SYSTEM WAS EXPLANTED **BECAUSE IT CAUSED CONSTANT PAIN AND JERKY MOVEMENT.** ANALYSIS IS ONGOING. ANALYSIS HAS SHOWN NO ANOMALY.
DT - DATE OF OCCURRENCE: 19930723
AN - ACCESSION NUMBER: 1272556

TX - TEXT: THE DEVICE WAS EXPLANTED DUE TO **"JOLTS ROUND THE GENERATOR SITE."** THE DEVICE WAS SENT BUT NOT RECEIVED FOR ANALYSIS (LOST IN TRANSIT); THEREFORE, THE REPORTED PROBLEM COULD NOT BE VERIFIED. NO DEATH OR SERIOUS INJURY HAS BEEN REPORTED.
DT - DATE OF OCCURRENCE: 19921109
AN - ACCESSION NUMBER: 1226340

TX - TEXT: PT EXPERIENCED **MASSIVE SHOCK (FROM THE TRANSMITTER) AND THE ASSOCIATED STIMULATOR CAUSED HER TO SHUT HER JAWS QUICKLY; CONSEQUENTLY SHE REQUIRED DENTAL TREATMENT.** THE CAUSE OF THIS EVENT HAS NOT BEEN DETERMINED. IN ADDITION, AVAILABLE FREQUENCY AND SEVERITY DATA DO NOT INDICATE THAT ANY FURTHER INVESTIGATION IS NECESSARY AT THIS TIME. BOTH THE FREQUENCY AND SEVERITY OF THIS EVENT WILL BE PERIODICALLY MONITORED TO DETERMINE IF ANY FOLLOW-UP AND/OR OTHER ACTION IS INDICATED.
DT - DATE OF OCCURRENCE: 19880620
AN - ACCESSION NUMBER: 1059301

After review of the type of events that can occur with this device and the patient sequelae, it should be concluded that the special controls proposed by the petitioner are not adequate to reasonably assure the safety and effectiveness of the device. We believe that the rigors of the PMA process (clinical and non-clinical testing, and inspection) are required prior to commercial release to assure that the device is safe and effective.

5. Literature

The literature regarding spinal cord stimulation from 1961 to 1999 is rich and includes retrospective and prospective series, review articles, basic science discussions, and case reports. Attachment C is a bibliography of the literature reviewed and Attachment D provides a summary of this literature, sorted by author. Quantity of patients, complications rates, device used, and conclusion are listed.

Two types of literature merit careful consideration. The first is retrospective and prospective series which appear to present quantifiable safety information (especially when controlled). Next we turn to review articles, which may offer insights into the long-term experience of seasoned practitioners in large institutions. While less quantifiable than series articles, review articles are valuable because they include a discussion about the management of risk and may aid in the understanding of safety. IPG safety, as reported in the literature, then, is about understanding the risk of what happens rarely, as well as what happens most frequently.

The 1995 meta-analysis of SCS by Turner, Loeser and Bell[1] sought to assess the relative safety of stimulator types:

> A vast majority (33) of studies involved single-channel stimulators, the only type available at the time most of the studies were conducted. Only one study used a multiple-channel stimulator, and four studies used both single and multiple channel stimulators. The type of stimulator could not be determined in one study...We attempted to compare complication rates of older systems versus those of currently used systems, but this was not possible given the extremely small number of articles that reported complications exclusively for patients with the newer quadripolar or octapolar systems.

Given this conclusion, and the changes in technology since that time, we view Turner's work as a pivotal point for discussions about IPG safety. The literature before 1995 is not poolable for comparative purposes. However, some early studies may contain useful data regarding safety. Advancements in clinical reporting post-1995 greatly increased the quality of safety discussions; this is especially significant in view of new technology.

Of the 72 series articles reviewed, we first reviewed those articles with an explicit discussion of stimulator type. We have defined stimulator type as a radio frequency (RF) device or an implantable pulse generator (IPG). Note that the number of cases of mixed and unknown stimulator type has decreased, while the number of studies identified as IPG studies has increased.

Table 7: Series before and after 1995, by stimulator type

	Number of articles	RF	IPG	Mixed	Unknown
Prior to 1995	42	18	6	12	6
1995 to present	30	7	16	6	1

We then reviewed complications, defined as: SCS-related problems such as; infection, cerebrospinal fluid leakage, pain at the wound site, and/or hematoma. It does not include

[1] "Spinal Cord Stimulation for Chronic Low Back Pain: A Systematic Literature Synthesis", Turner, Loeser and Bell, Neurosurgery, volume 37, number 6, (December 1995).

We then reviewed complications, defined as: SCS-related problems such as; infection, cerebrospinal fluid leakage, pain at the wound site, and/or hematoma. It does not include problems related to lead placement or hardware failure, nor does it include unsatisfactory therapy efficacy. Please note three findings. Relative to the total number of studies, the average rate of complications as a percentage of implants has decreased and the number of studies providing complications discussion has decreased. And, please note that IPG-specific complications, as reported in the literature, have increased since the period prior to 1995.

Table 8: Series before and after 1995, summary of complication

	Articles	Complication discussion	**Complications as a percentage of implants (average)**	IPG-related complications
Prior to 1995	42	36	**5.93%**	6
1995 to present	30	19	**5.23%**	20

Of the 72 series reviewed between 1961 and 1999, 34 studies (16 before 1995, 18 since 1995) include information about both the stimulator used and the complications experienced. Table 8 demonstrates that the overall complication rate has decreased slightly since 1995.

As stated previously we believe literature before 1995 is difficult to consider in regard to a comparative quantitative analysis. Comparisons continue to remain difficult post-1995, based on the lack of complications reported using similar definitions. Thus, our overall review of these articles is inconclusive.

6. Conclusion

After review of:

- The description of radio frequency (RF) devices compared to internal battery pulse generators (IPG),
- The discussion of predecessor devices and related regulatory history, and
- The discussion of comparative/similar devices and related regulatory history.

And review of:

- Adequate MDR descriptions, and
- The literature review.

We believe it can be concluded that the petitioner's proposal has not demonstrated reasonable assurance that reclassification of these devices from Class III to Class II will adequately protect public safety. Reclassification would allow a significant loss in the amount of control that is currently in place, and result in an increase in the level of risks to the patient.